Original Article

Impact of Spectral Severity of Alcoholism on Visual-Evoked Potentials: A Neuropsychiatric Perspective

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Abstract

Background: The deleterious effects of alcohol on the brain are replete in literature. Only a few neurophysiologic measures can pick up the neuronal dysfunctions, one of them being visual-evoked potential (VEP). A very limited amount of data exists on the progression of neural abnormalities related to the spectral severity of alcoholism. **Aim of the Study:** To evaluate the impact of spectral severity of alcoholism through VEP and to understand the emergence of any specific pattern or morphometric abnormalities related to alcohol-induced neuropsychiatric presentations. **Methodology:** A total of 90 cases were recruited in addition to 180 age- and sex-matched controls using purposive and random sampling. The Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version and Campbell Neuropsychiatric Inventory were used to evaluate alcohol disorders and its neuropsychiatric complications apart from the mandatory consultant-specific clinical evaluations of all the cases. Of 90 cases of alcohol dependence, 15 patients were currently abstinent for >6 months, 15 had alcohol intoxication, 15 had signs of alcohol withdrawal, 15 had physical complications, 15 had psychiatric comorbidity, and 15 had neurological complications such as epilepsy. VEP recordings were taken using an Evoked Potential Recorder (RMS EMG. EP MARK II) where the stimulus configuration consisted of transient pattern-reversal method in which a black and white checkerboard was generated full field. **Results:** Mean age of cases was 37.71 ± 11.49 years compared to 39.43 ± 10.67 years in controls (range 18–65 years). VEP abnormalities comprising of prolonged latencies (62.5%) with a statistically significant difference ($P < 0.001$) from the healthy controls was observed in cases of alcohol withdrawal syndrome. Predominant amplitude reduction with normal latency was obtained in 37.5% cases of withdrawal. Severe VEP abnormalities, i.e., both latency delay and amplitude reduction, were found in 75% patients with psychiatric comorbidity, 66.67% patients with neurological complications, i.e., epilepsy, and 33.34% patients with physical complications. An explicit finding of prominent interocular differences was a prominent feature present in 25% of patients with complications.

Keywords: *Alcohol dependence, amplitude, latency, neuropsychiatric, psychiatric complications, visual-evoked potential, withdrawal*

Introduction

Alcohol (ethanol) is one of the most widely misused drugs in both developed and developing countries. Neural functional pathologies may exist in alcohol addicts even when no obvious clinical manifestations are apparent. Neural functional pathologies may also exist where fatal complications are evident. In the National Comorbidity Study, 29.2% of respondents with

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alcohol dependence experienced either an independent or a substance-induced mood disorder within the past 12 months of their assessment, a rate that was 3.9 times higher than those who were not alcohol dependent. Bipolar disorder over the previous year was seen in 1.9% of the respondents with alcohol dependence, a rate 6.3 times greater than nonalcoholics.[1-3] Thus, factors leading to these observed/induced changes are poorly understood, and there are hardly any ways or means to predict who would develop neural insults and who would not. The question that remains is – If alcohol itself causes insult to the brain and to what extent it can be picked up early? Can we detect or measure the continuity or progressive involvement in any way? The best models used in understanding alcohol-induced brain damage have been retrieved from the studies related to alcohol-induced optic neuropathy, encephalopathy, or seizures. For example, patients with alcohol-related optic neuropathy present with a bilateral, progressive, painless loss of visual acuity, dyschromatopsia, and subsequent disc changes including marked temporal disc pallor and retinal nerve fiber layer loss mainly in the papillomacular bundle. Early detection and prompt management may decrease visual impairment and aid in reversing the optic nerve damage and revival in visual status.[4] It has been achieved clinically with the use of visual-evoked potential (VEP), which serves as an important means of obtaining reproducible, qualitative, and quantitative data on the function of the visual pathways and the visual cortex.[5]

A few studies have reported changes in VEP following alcohol consumption. A study in Spain found that the amplitude of VEP increases with pattern reversal, at a blood alcohol level (BAL) of 0.8 g/kg.[6] In the USA, Krull *et al*.[7] found that alcohol increases the latency of a 250-ms negative component (N2) only in the absence of sleep deprivation. Other studies found no correlation between the level of alcohol consumption and VEP parameters for the first deflection.[8] Quintyn *et al*.[9] studied changes in the vision of 16 people after consumption of a small quantity of alcohol. Their results indicated that alcohol consumption caused no significant difference in performance. Further, VEP has also been shown to identify how its specific morphological pattern depending on BAL can help us know the severity of the brain involvement. Visual target detection in a treatment-naïve alcohol-dependent (TNAD) sample versus age and gender comparable nonalcoholic controls was investigated by Fein and Andrew.[10] The significant reduction in P3b amplitude in TNAD reflected the effects of active alcohol abuse.

Petit *et al*.[11] have concluded that elevated alcohol cue reactivity may lead to poorer inhibitory performance in heavy social drinkers and may be considered as an important vulnerability factor in developing alcohol misuse when assessing event-related potentials (ERPs) in them.

Another ERP study by Petit *et al*.[12] showed that reduced processing of alcohol cues predicts abstinence in recently detoxified alcoholic patients in a 3-month follow-up period. Abstainers presented with decreased P3 amplitude in this study.

While alcohol dependence is associated with augmented automatic attentional biases early in processing, escape drinking was found to be related with more controlled attentional biases to active alcohol cues during a relatively later stage in processing. This was reported in a recent study by Dickter *et al*.[13]

Recently, occipital ERPs to addiction-related stimuli in detoxified patients with alcohol dependence and their association with 3-month relapse were studied by Matheus-Roth *et al*.[14] Their results indicated a sensitivity of occipital ERPs to addiction-related stimuli.

However, scanty data exist for the utility of VEP on the progression of neural abnormalities related to spectral severity of alcoholism when it comes to neuropsychiatric implications.

There is a dire need for a study which can explore comprehensively or conceptually empirical evidence or a neurophysiological biomarker which could help us develop preventive vigilance for identifying those who could develop such neuropsychiatric complications. In this context, the present study aimed at evaluating the impact of spectral severity of alcoholism through VEP to understand the emergence of any specific pattern or morphometric abnormalities related to alcohol-induced neuropsychiatric presentation.

Objectives

1. To screen the patients by both clinical and neurophysiological evaluations for the spectral severity of alcoholism
2. To identify specific patterns emerged between spectral severity and to determine temporal association of VEP abnormalities in patients on spectral severity of alcoholism.

Methodology

Setting

Outpatient and inpatient services of the Department of Psychiatry, Department of Medicine, and Department of Surgery in our tertiary care rural hospital were the study setting.

Place of the study

Neurophysiology unit, Department of Physiology, Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha, Maharashtra, was the place of the study.

Study design

This was a cross-sectional, observational, noninterventional, single-time assessment, hospital-based study.

We used purposive and random sampling to determine the samples.

A total of 90 cases (15 patients each in 6 subgroups) of patients on spectral severity of alcohol use disorder with physical/neuropsychiatric complications and 180 age- and sex-matched controls were recruited after screening 668 patients of alcohol dependence syndrome visiting either to the Department of Psychiatry, Medicine, or Surgery of our tertiary care rural hospital for studying VEP abnormalities.

Ninety cases of alcohol dependence were divided into six following groups:

i. Fifteen patients of alcohol dependence syndrome who were currently abstinent for >6 months
ii. Fifteen patients had alcohol intoxication and were under treatment for the last 72 h
iii. Fifteen patients who had signs of alcohol withdrawal syndrome and were admitted to psychiatric inpatient services
iv. Fifteen patients who had physical complications related to liver (hepatic encephalopathy secondary to alcoholic cirrhosis) and were admitted to inpatient services of either of medicine or surgery
v. Fifteen patients who had psychiatric comorbidity of alcohol-induced mood disorder/psychotic disorder after stopping alcohol for more than a month and were admitted to the inpatient services of psychiatry.
vi. Fifteen patients who had neurological complications such as epilepsy induced by alcohol use disorder and who were evaluated just before/within a day of starting antiepileptics.

The healthy 180 controls who were age and sex matched were also screened for any abnormalities before neurophysiological evaluation. All participants reported normal or corrected-to-normal vision, wherever possible, and this was corroborated by medical records. Controls were free of any psychiatric illness or symptoms, and they reported no history of alcohol or substance abuse in the last 5 years or more.

Only those participants who fulfilled the inclusion criteria were selected.

Inclusion criteria

The men aged 18–60 years were included in the study. The patients who were diagnosed as chronic alcoholics according to the strict Diagnostic and Statistical Manual-IV (DSM-IV-TR)[15] criteria developed by the American Psychiatric Association for the clinical diagnosis of abuse and dependence were included. The presence of family history of alcoholism in the first- or second-degree relative and those patients who are physically stable enough to undergo VEP and competent and willing to give informed consent were also included in the study.

Exclusion criteria

The patients with lens/corneal opacities, miotic pupil, and recent eye medications (mydriatics or cycloplegics in the past 12 h); patients with serious systemic illness affecting the performance of VEP, history of other neurological disorder, or heart disease; patients with subnormal intelligence, history of comorbid diagnosed neurological disorders such as epilepsy or neurodegenerative disorders, comorbid substance abuse, except minimal nicotine use; patients with history of head injury or patients having undergone recent neurosurgery, Suicidal/homicidal/catatonic patients, presence of tardive dyskinesia/antipsychotic-induced movement disorders, those not willing for study participation or whosoever refused to be a part of our study; patients with any history of visual impairment beyond corrected-to-normal vision; patients with any uncooperative or febrile patient were not included in the study.

Recruitment/assessment of participants

This was done under two heads namely clinical analysis and neurological evaluation.

Clinical analysis

Sociodemographic profile sheet was filled for each subject, and psychiatric status of alcoholic patients was assessed using Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version[16] and Campbell Neuropsychiatric Inventory for additional neuropsychiatric complications apart from consultant-specific clinical evaluation for all cases were done by a consultant psychiatrist.

Neurophysiological evaluation

All the participants were evaluated for transient pattern-reversal VEP by a neurophysiologist.

Procedure of visual-evoked potential recordings

Transient-pattern reversal VEP (PRVEP) recordings were done in accordance with standardized methodology of the International Federation of Clinical Neurophysiology Committee Recommendations[17] and International

Society for Clinical Electrophysiology of Vision Guidelines,[18] and montages are kept as per 10–20 International System of Electroencephalography electrode placements keeping the reference electrode (Fz) placed 12 cm above the nasion, the ground electrode (Cz) at the vertex, and the active electrode (Oz) at approximately 2 cm above the inion.

The electrode impedance was kept below 5 KΩ. The stimulus configuration consisted of the transient pattern-reversal method in which a black and white checkerboard is generated (full field) on a VEP Monitor by an electronic pattern regenerator inbuilt in an Evoked Potential Recorder (RMS EMG. EP MARK II manufactured by Recorders and Medicare Systems, Chandigarh). The rate of pattern reversal (1.7 Hz), the size of the checks (8 × 8), the luminance (59 cd/m^2), and contrast level (80%) were kept constant for all the recordings in all the cases. The recording was done monocularly for the left and right eyes separately with the participant wearing corrective glasses if any during the test. If the cooperation of the participant or fixation stability was poor, the VEP recording was repeated after 5 min break. If the recorded signal was suboptimal, the VEP recording was repeated until a satisfactory recording was achieved.

Ethics consideration

The research protocol for the present study was submitted to the Institutional Ethics Committee, and we received ethical clearance before the commencement of the study. Informed consent was submitted by all participants before the investigation. All research and data collection protocols complied with the Declaration of Helsinki.

Statistical analysis

SPSS 23.0 Version, (IBM, USA) was used to enroll sociodemographic and clinical variables for both case (s) and control and to carry out descriptive and inferential statistics. One-way ANOVA was used to test significant differences between the six groups. Significant differences between each paired groups were then evaluated by *post hoc* Tukey's test.

Results

A total of 668 sample subjects were screened for obtaining 15 patients each in six subgroups of alcohol spectral severity for studying VEP abnormalities. The mean age of 90 cases of alcohol dependence was 37.71 ± 11.49 years while that of 180 healthy age- and sex-matched volunteers was 39.43 ± 10.67 years while their mean age did not differ significantly and both groups were comparable for age and gender as seen from Table 1. Among six different subgroups of alcohol use disorder/related complications, participants who had physical complications were found to be the oldest among six subgroups with mean age of 47.67 ± 15.53 years while those who have been abstinent for more than 6 months were the youngest (31.20 ± 4.55 years). Mean age of onset for psychiatric comorbidity was far earlier (33.75 ± 13.45 years) than both central nervous system (CNS)-induced complications (42.67 ± 4.04 years) and physical complications.

Tables 2 and 3 show quantitative analysis of VEP using one-way ANOVA for six subgroups so as to identify which of them (N70 latency, P100 latency, N155 latency, and P100 amplitude) might have significant impact on differentiating six subgroups of alcohol spectral severity. We found N70 latency getting significant and distinctive findings in the subgroups of physical complications and psychiatric comorbidities. However, P100 latencies were found to be significantly prolonged in alcohol intoxication, alcohol withdrawal, alcohol-induced physical, psychiatric and neurological complications; therefore, P100 latency delay could be a common, but indistinguishable pathway for alcohol-induced neural insults as observed in our study. When we further compared N155 latencies among these six subgroups, only those with hepatic encephalopathy (physical complications) were found to have highest delay and could be significantly differentiated from the other subgroups. Going a step further, P100 amplitude was significantly lower in patients of alcohol withdrawal and patients of hepatic encephalopathy and alcohol-induced epilepsy, providing us another matrix of association wherein dual associations could be formed. Thus, P100 latency delay and P100 amplitude reduction both are found to be significant only in the subgroup of alcohol-induced epilepsy which can be differentiated from the subgroup of intoxicated patients where

Table 1: Mean±standard deviation of age and duration of abuse in all the study groups

Group	Category	Mean±SD	
		Age (years)	Duration of abuse (years)
I	Abstinent	31.20±4.55	2.40±0.55
II	Intoxicated	38.14±12.52	4.57±1.72
III	Withdrawal	36.29±12.53	6.21±2.61
IV	Physical complications	47.67±15.53	15.67±2.08
V	Psychiatric comorbidity	33.75±13.45	17.50±4.04
VI	Epilepsy (CNS complication)	42.67±4.04	18.67±1.15

CNS: Central nervous system, SD: Standard deviation

P100 amplitude reduction is insignificant, and alcohol withdrawal patient can be differentiated from the patient of alcohol-induced epilepsy when N70 latency parameter has been used.

All these quantitative results are also depicted in Figure 1.

Nevertheless, as shown in Table 4, not all patients necessarily resulted in such observations. The relative percentage of abnormal waveform morphology, latency delay, and amplitude reduction could be segregated with variable quantum of patients, for example, predominantly extended latencies (62.5%) with a statistically highly significant difference ($P < 0.001$) as compared to healthy controls were observed in cases of alcohol withdrawal syndrome while severe VEP abnormality as in both latency delay and amplitude reduction was found in 75% patients with psychiatric comorbidity and 66.67% patients with neurological complications. Interestingly, an explicit finding of prominent interocular differences was a feature present in 25% of patients with complications. Finally, abnormal waveform morphology, poorer reproducibility, and differentiation ability of the evoked complex which frequently had an atypical shape were obtained in 33.34%. A composite view of representative waveforms obtained in each group is illustrated in Figure 2.

Discussion

Alcohol-induced physical/neuropsychiatric complications are etiologically and phenotypically complex. It is evident that a chronic alcohol exposure typically leads to Vitamin B12 or folate deficiency, and over a time, these deficiencies cause accumulations of formic acid and its derivatives, which further inhibit(s) the electron transport chain and mitochondrial function, resulting in the disruption of Adenosine Triphosphate (ATP) production and ultimately impairing the ATP-dependent axonal transport system. Clinicians often need to detect early complications or ideally pick up vulnerable patients for whom such complications are likely to happen in the near future; however, unfortunately, there are hardly any biologically identifiable ways/markers to discern such disposing states. The acute effects of alcohol on the visual cortical/neural system have previously been evaluated with VEP;[6-8,19-22] some of them validated VEP to help in differentiating from normal or alcoholic withdrawal patients, but none of them ever thought for spectral severity or set of specific emerging VEP patterns that might predict the endophenotypic state of the alcohol-induced neuropsychiatric complications. The N75, P100, and N135 components are found to be generated from the striate cortex (V1) or the extrastriate cortex. Alcohol-induced

Table 2: Integration of quantitative results of visual-evoked potential latencies (ANOVA)

Group	Category	N70 Latency (m)			*F*	P100 Latency (m)			*F*	N155 Latency (m)			*F*
		Mean±SD	95% CI for mean		*P*	Mean±SD	95% CI for mean		*P*	Mean±SD	95% CI for mean		*P*
			Lower bound	Upper bound			Lower bound	Upper bound			Lower bound	Upper bound	
I	Abstinent	72.72±3.56	70.17	75.27	2.49	102.66±4.32	99.56	105.75	5.359	142.79±5.82	138.62	146.95	1.58
II	Intoxicated	75.80±4.56	71.00	80.59	0.042	107.63±2.033	105.50	109.77	0.001	146.34±3.90	142.24	150.44	0.18
III	Withdrawal	76.85±6.07	73.34	80.36	(S)	110.52±5.73	107.21	113.83	(S)	151.44±9.20	146.13	156.75	(NS)
IV	Physical Complication	81.49±7.49	73.62	89.36		118.22±7.22	110.64	125.79		154.38±14.35	139.32	169.44	
V	Psychiatric co-morbidity	80.20±6.52	74.74	85.66		109.91±5.158	105.61	114.22		152.10±12.51	141.64	162.56	
VI	Epilepsy	72.66±9.63	67.10	78.23		103.81±10.42	97.79	109.83		143.76±16.42	134.27	153.24	

SD: Standard deviation, CI: Confidence interval, S=Significant, NS=Not significant

Table 3: Integration of quantitative results of visual-evoked potential amplitude (ANOVA)

Group	Category	P100 amplitude.(μvolts)			*F*
		Mean±SD	95% CI for mean		*P*
			Lower bound	Upper bound	
I	Abstinent	6.47±3.09	4.2672	8.6908	2.429
II	Intoxicated	4.71±3.68	0.8448	8.5852	0.047 (S)
III	Withdrawal	4.04±1.61	3.1130	4.9784	
IV	Physical complication	3.45±0.17	3.2649	3.6417	
V	Psychiatric comorbidity	4.62±2.23	2.7591	6.4934	
VI	Epilepsy	3.68±1.42	2.8670	4.5073	

SD: Standard deviation, CI: Confidence interval, S: Significant

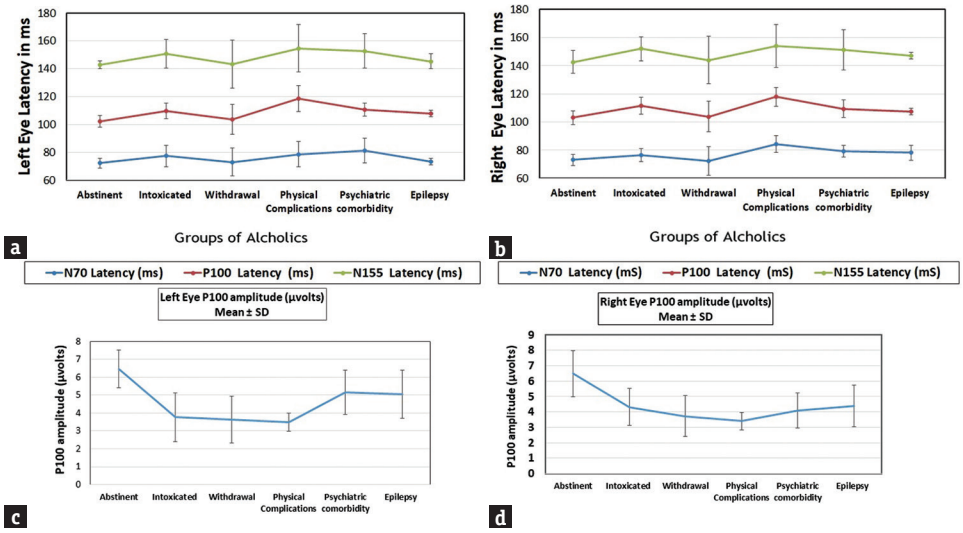

Figure 1: Integration of quantitative results . (a) VEP Latencies of left eye, (b) VEP Latencies of right eye, (c) P100 amplitude in left eye, (d) P100 amplitude in right eye

Table 4: Relationship of visual-evoked potential responses with spectral severity of alcoholism

Group	Category	*n*	Percentage of cases with predominant latency delay (amplitude WNL)	Percentage of cases with predominant amplitude reduction (latency WNL)	Percentage of cases with both latency delay and amplitude reduction	Percentage of cases with abnormal waveform morphology	Percentage of cases with normal waveform
I	Abstinent	15	0	0	0	0	100
II	Intoxicated	15	100	0	0	0	0
III	Withdrawal	15	60	40	0	0	0
IV	Physical complications	15	13.33	20	66.67	0	0
V	Psychiatric comorbidity	15	13.33	6.66	73.34	6.66	0
VI	Epilepsy	15	26.66	6.66	33.33	33.33	0

WNL: Within Normal Limits

CNS suppression and nerve conduction delay have been reported to be mediated by gamma-aminobutyric acid (GABA), glycine, and adenosine.[23] GABA and glycine are the main inhibitory neurotransmitters in the CNS. Alcohol also increases the level of adenosine, which contributes to the sedative actions of alcohol. Furthermore, interactions of alcohol with myelin or the Ca-ATPase pump at the synapses also may explain these neurophysiological changes.[24] Thus, our study is the first one documented to evaluate and putatively search for optimal neurophysiological biomarkers for differentiating alcohol spectral severity by empirically identifying specific set of patterns obviously discernable (if any) on VEP in six divided set of subgroups of patients. The previous data from >20 studies[9,25-35] [Table 5] showed few robust pointers for usefulness of VEPs in relation to alcohol use disorder (s) not only in *in vivo* animal experimentations but also in humans helping to differentiate subgroup of patients who had been abstinent for more than 3 months to those who are either intoxicated or having withdrawal. To our surprise, we noted couple of critical studies by Urban *et al*. and Nazliel *et al*., who reported that only 28% and 15% of alcoholics had abnormal findings on VEP, which is in contrast to most studies including ours with 75% patients with psychiatric comorbidity and 66.67% patients with neurological complications. Certainly, this is very unique way of neurophysiological differentiation on spectral severity of alcoholism as observed and conceptually derived for the first time ever in the literature [Table 4] from our study. Nevertheless, such relative percentage of abnormal waveform morphology, latency delay, and amplitude reductions in VEP as biomarker clearly holds us back in reaching to unified consolidative neurobiological markers until our understanding and technological advances get widen in the future. An ultimate and implicit goal of the work described in this article is to develop more effective prevention techniques. Increased understanding of the biological mechanisms and genetic impact associated with a specific type of increased vulnerability to alcoholism could enhance prevention

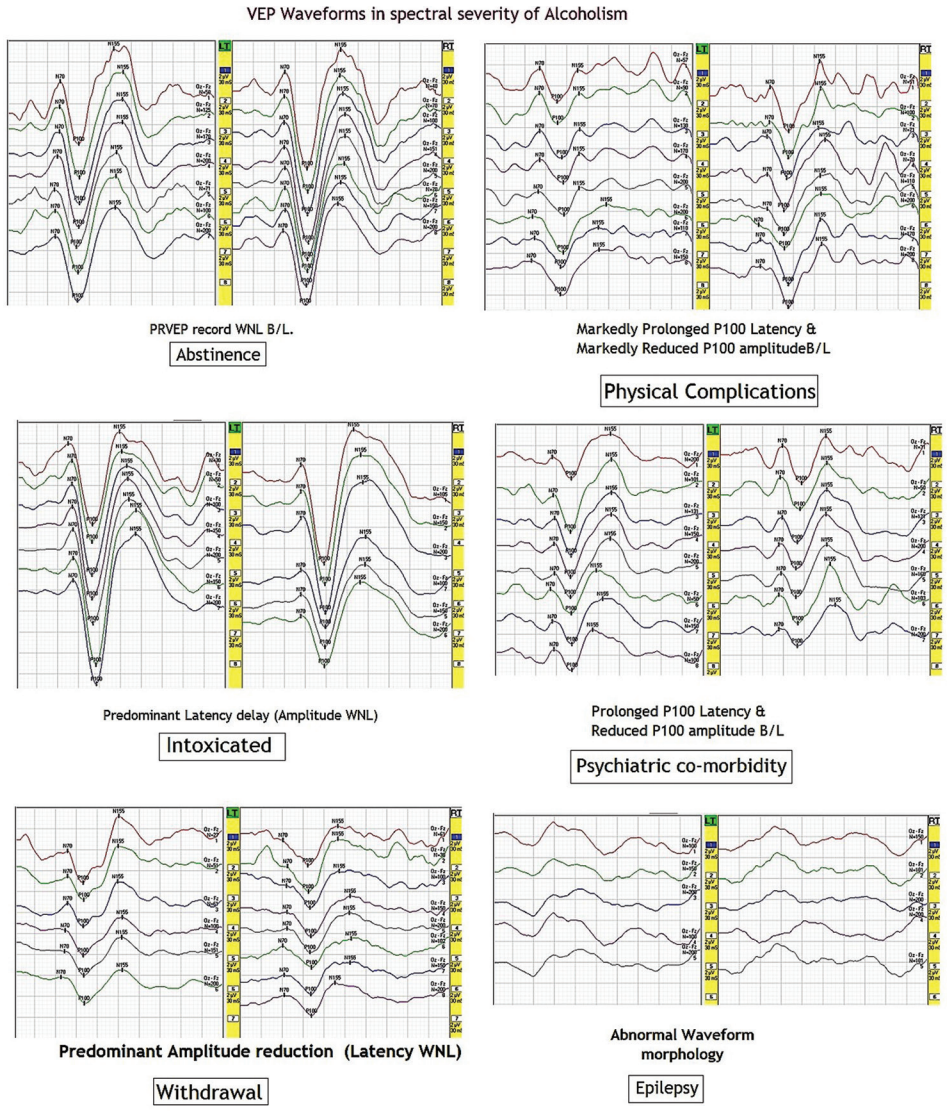

Figure 2: Visual-evoked potential waveforms in the spectral severity of alcoholism

efforts in several ways. For instance, PRVEP abnormalities obtained in asymptomatic chronic alcoholics of our study suggest that they may be useful in the detection of early changes and in following the progress of cases with the chronic addiction. This study adds further evidence and emphasis to the sparse literature of usefulness of VEP in a wide spectrum of alcohol abuse seen in young adults. This also helps to establish the importance of a visual electrophysiological evaluation as a valuable adjunct to detailed psychiatric assessment of alcoholics and provides a decent recommendation for VEP to be a part of their routine examination as it might be a useful marker which may help to clearly classify the spectral severity of alcoholism and help in early rehabilitation of addicts.

Given the multiplicity of experimentally driven and empirical clinical findings of VEP in spectrum of alcoholism, we could elucidate the ingredient of progressively more profound and consistent observable patterns of association that might potentially differentiate the kind of variety of alcohol-related spectra. The importance of a neurophysiological marker's (VEP) precision, accuracy, sensitivity, and specificity cannot be overemphasized. Although it is unlikely that researchers will find a single marker to satisfy all clinical needs, they may eventually develop combinations of markers for specific clinical purposes, from unselective screening (i.e., drinking versus not drinking) to confirming a suspicion of alcohol induced. The conceptual overview espoused here is ripe for both further preclinical experimental testing and exploratory therapeutic interventions. Should this prove to be true, our findings we believe would contribute to a stronger basis for clinical care and a more objective assessment of alcohol-related complications or help in identifying that might relapse or would have neuropsychiatric

Table 5: Comparison of various studies related to alcohol use disorder and visual-evoked potentials

Investigator (s)	Year	Sample	Brief finding(s)
Coger *et al*.[25]	1976	17 alcoholics in withdrawal, 27 stabilized alcoholics, and 30 control volunteer subjects	Significantly greater abnormal evoked response amplitudes in withdrawal compared to stabilized alcoholics
Taghavy *et al*.[26]	1976	VEP to stimuli of 1" per sec was applied to 16 normal individuals	Amplitude of N2-P3 (120-170 m after the stimuli) was depressed in all. The latencies of N2 and P3 were increased concurrently. The latency of P3 was increased by 10.7%
Zuzewicz[27]	1981	30 clinically healthy pilots who were given 1 g/kg of body weight of ethanol orally. VEPs were recorded 30 and 60 min after alcohol ingestion	Prolongation of the latency of all components with rising concentration of ethanol in the blood. VEPs showed three types of individual reactions to ethanol: Type I - Increasing reduction of amplitude of components with rising blood alcohol concentration; Type II - Rising amplitude, mainly of the late components; Type III - amplitude rise in the 30th min followed by amplitude fall in the 60th min without reaching, however, the initial level
Simpson *et al*.[28]	1981	Effects of ethyl alcohol on evoked potentials were studied in 12 healthy volunteers	Alcohol significantly reduced the amplitude and prolonged the latency of the N2-P2 components of the flash-evoked potential
Ahmed and Hines[29]	1983	VEPs were obtained in 19 patients during the early phase of alcohol intoxication	Out of 38 responses recorded in the 19 patients, 13% were found to be abnormal (5 responses). In 3 patients, major positive peaks returned to normal after treatment
Jensen and Krogh[8]	1984	12 eye healthy test persons were followed for 2 h after alcohol intake. Transient VER's were recorded with a stimulus of 14' and 110' check size	Increase in latencies after alcohol intake, but only in one stimulus modality (2 shifts per s, 14' check size) was the deviation statistically significant. No correlation between the level of alcohol consumption and VEP parameters for the first deflection
Kelley *et al*.[30]	1984	PRVEP recorded in normal subjects and alcoholics during withdrawal and repeated after 3 weeks of detoxification	N76 latency was longer in the alcoholic patient in the withdrawal phase than in the normal subjects. The latency returned to normal range after detoxification in younger alcoholic patients but did not in the older alcoholics
Meinck *et al*.[20]	1986	80 chronic alcoholics and in 43 normal subjects	P2 latencies and inter-eye differences were found above the 98% confidence limit in 30%, and above the 99.9% confidence limit in 10% cases. An abnormal waveform was observed in 12.5% and 7.5% of the patients
Emmerson *et al*.[31]	1987	VEPs were recorded from 60 males aged 25-40 (20 abstinent alcoholics, 20 social drinkers, and 20 lifetime on-drinkers). Alcoholics were at least 1 month abstinent, medication-free, neuropsychologically normal	Residual effects of alcohol abuse were not detected in VEP amplitude, latency, and amplitude/intensity slope measures
Devetag[32]	1988	13 chronic alcoholics who are currently drinking alcohol and 11 chronic alcoholics who had abstained for at least 1 year	Constant involvement of the VEP especially of the earliest component N70 and of the amplitude of the response. For the visual damage to withdrawal seems to determine a regression, only partial in nature. Optic nerve damage is a very rare event in alcoholism
Pollock *et al*.[33]	1988	The biological sons of male alcoholics, deemed to be at HR for the development of alcoholism, were compared to control males, aged 18 to 21 years, using measures of the VEPs elicited by checkerboard pattern reversal	HR subjects showed more symmetry in a positive component with approximate latency of 242 m compared with control subjects
Urban *et al*.[19]	1989	PRVEPs with checkerboard pattern investigated in 25 chronic alcoholics (24 men, 1 woman, mean age 45 years, mean period of abuse 26 years) and compared with control group of 46 healthy subjects	Abnormal finding of VEP was recorded in 28% of the alcoholics. The mean amplitude of VEP in the two groups did not differ significantly

Contd...

Table 5: Contd...

Investigator (s)	Year	Sample	Brief finding (s)
Colrain *et al*.[22]	1993	5 alcohol dose conditions were administered to 10 male subjects: 0.00 (placebo); 0.28; 0.36; 0.54 and 0.72 g/kg total body weight. EEG responses to a reversing checkerboard stimulus were measured	Changes in VEP following alcohol consumption, depending on blood alcohol level. Latencies of the P1 and P2 components of the VEP were unaffected. Latencies of N2 and P3 displayed significant dose-related increases with increasing blood alcohol levels. RMS power of the P3 complex was reduced by higher alcohol doses, as was the N2-P3 amplitude difference at central and parietal sites
Krull *et al*.[7]	1993	Effects of two levels of alcohol intoxication on visual the event-related potential (ERP) waveforms in 54 normal male subjects	Alcohol increases the latency of a 250 m negative component (N2) at 0.8 g/kg BAL but only in the absence of sleep deprivation
Azcona *et al*.[6]	1995	Interactions of alcohol and caffeine were studied in 8 healthy subjects	Decreased amplitude and increased latency in the VEP pattern (BAC, 0-20 mM/L; 0-0.09 vol%)
Post *et al*.[34]	1996	In the first experiment, 48 adult volunteers (33 females) responded to either the onset or offset of one of the five potential targets without alcohol to determine the relative demands on attention of stimulus onset and offset. The spatial extent of the five-target display was also varied. In the second experiment, the effect of alcohol was determined for both the onset and the offset tasks in 12 adult volunteers (9 females)	A statistically significant increase in the latencies of P2 The results indicate that alcohol impairs performance on tasks that place greater demands on visual spatial attention and likely disrupts the ability to shift attention from one spatial locus to another during serial search
Quintyn *et al*.[9]	1999	Changes in the vision of 16 people after consumption of a small quantity of alcohol was studied	Visual performance is less affected by the visual changes than by alteration in brain functions for a low blood alcohol level
Nazliel *et al*.[21]	2007	40 study patients who had histories of alcohol abuse for at least 6 years	15% of the patients demonstrated abnormal VEP results at least in one tested eye
Kim *et al*.[35]	2016	VEP (0.25 pattern sizes) were performed on 15 healthy before ethanol administration Ethanol (0.75 g/kg) was administered orally over the course of 30 min. VEP and blood alcohol concentration were evaluated 1 h after ethanol administration	The latency and amplitude of N75, P100, and N135 were measured. VEP revealed a P100 latency delay (109.4±5.3; 113.1±8.2; P=0.008) after alcohol administration
Kothari *et al*	2017	A total of 90 cases of patients on spectral severity of alcohol use disorder with physical/ neuropsychiatric complications and 180 age- and sex-matched controls were recruited using purposive and random sampling after duly obtaining their consent. A total of 668 sample subjects were screened for obtaining 15 patients each in six subgroups of alcohol spectral severity for studying VEP abnormalities	Predominantly extended latencies (62.5%) with a statistically highly significant difference (P<0.001) as compared to healthy controls was observed in cases of alcohol withdrawal syndrome. Predominant Amplitude reduction with normal latency was obtained in 37.5% cases of withdrawal. Severe VEP abnormality as in both latency delay and amplitude reduction was found in 75% patients with psychiatric comorbidity and 66.67% patients with neurological complications, i.e., epilepsy, 33.34% patients with physical complications Abnormal waveform morphology, poorer reproducibility, and differentiation ability of the evoked complex which frequently had an atypical shape were obtained in 33.34%

VEP: Visual evoked potential, VER: Visually evoked pattern response, PRVEP: Pattern reversal visual-evoked potential, HR: High risk, EEG: Electroencephalogram, ERP: Event-related potentials

complications in the future and such phenomena deserve explorations.

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Conflicts of interest

There are no conflicts of interest.

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